In the United States Court of Federal Claims

ANGELICA VINESAR and MARIUS VINESAR as best friends of their daughter, A.V.,	)	
Petitioners,	)	No. 18-440V (Filed Under Seal: March 6, 2024; Re-issued: March 25, 2024)*
v.	)	
SECRETARY OF HEALTH AND HUMAN SERVICES,	)	
Respondent.	)	

John F. McHugh, New York, NY, for Petitioners.

Julia M. Collison, Assistant Director, Torts Branch, Civil Division, U.S. Department of Justice, with whom were Lara A. Englund, Assistant Director, Heather L. Pearlman, Deputy Director, C. Salvatore D'Alessio, Director, and Brian M. Boynton, Principal Deputy Assistant Attorney General, for Respondent.

OPINION AND ORDER

KAPLAN, Chief Judge.

Petitioners in this case, Angelica L. and Marius Vinesar, seek review of the decision of Special Master Christian Moran finding that they failed to prove that their daughter, A.V., suffered a vaccine-related injury that would entitle her to compensation under the National Childhood Vaccine Injury Act of 1986, 42 U.S.C. §§ 300aa–1 to –34 ("Vaccine Act" or "Act"), as amended. See Decision of Spec. Mstr., ECF No. 136 [hereinafter "Dec."]; see also Vinesar v. Sec'y of Health & Hum. Servs., No. 18-440V, 2023 WL 5427935 (Fed. Cl. Spec. Mstr. July 28, 2023). Specifically, they challenge the Special Master's findings: (1) that they did not establish by preponderant evidence that the diphtheria-tetanus-acellular pertussis ("DTaP") vaccine A.V. received in April 2015 caused her to develop Dravet syndrome (a seizure disorder); (2) that the DTaP vaccine did not significantly aggravate her pre-existing genetic susceptibility to developing Dravet syndrome, see Dec. at 52; and (3) that, in any event, the Secretary of Health

* Pursuant to Vaccine Rule 18(b) of the Court of Federal Claims, the Court initially filed this opinion and order under seal on March 6, 2024, and the parties were afforded fourteen days to propose redactions. Neither party proposed any redactions. The Court therefore publicly reissues the opinion and order initially filed under seal without any redactions.

and Human Services ("Secretary") demonstrated by preponderant evidence that a pathogenic genetic mutation was the sole cause of A.V.'s Dravet syndrome, see id. at 74.

For the reasons set forth below, the Court concludes that the evidence of record taken as a whole supports the Special Master's decision and that his conclusions are neither arbitrary and capricious nor contrary to law. Petitioners' Motion for Review, ECF No. 143, must therefore be denied.

BACKGROUND

I. Medical History

A. A.V.'s First Febrile Seizure

A.V. was born without complications or medical problems on September 23, 2014. Pet'rs' Ex. 1, at 1, ECF No. 1-2. Newborn screening and the physical exam completed the day after her birth were normal. See Pet'rs' Ex. 9, at 25–33, ECF No. 12-2.

Some seven months later, on April 20, 2015, A.V. underwent a periodic well-child check-up. Pet'rs' Ex. 11, at 30, ECF No. 12-4. During that check-up, A.V. received her third scheduled dose of the DTaP vaccine along with additional doses of the standard panel of recommended childhood vaccines. See id.; Pet'rs' Ex. 8, at 1, ECF No. 12-1. Just over twelve hours later, A.V. experienced a seizure. Pet'rs' Ex. 3 pt. 1, at 36, ECF No. 1-4 (Apr. 20, 2015). Ms. Vinesar called 911. Id. The emergency responders ("EMS") administered the sedative Diastat (diazepam) to A.V. while en route to the hospital. Id. at 32.

About ten minutes after her arrival at the hospital, A.V.'s seizure-like activity resumed and she was given another dose of diazepam. See id. Her temperature was recorded as 101.1° Fahrenheit. See id. (recording A.V.'s temperature as 38.4° Celsius). A computerized tomography ("CT") scan of A.V.'s head was taken and interpreted as unremarkable. See Pet'rs' Ex. 3 pt. 2, at 88, ECF No. 1-5. No signs of infection appeared on A.V.'s chest x-ray or in the results of rapid blood tests. See id. at 85–86, 89.

A.V. was admitted to the hospital with a diagnosis of complex febrile seizures. See Pet'rs' Ex. 3 pt. 1, at 32. Based on A.V.'s history, physical exam, and the diagnostic studies completed in the emergency department ("ED"), A.V.'s attending physician concluded that the vaccinations A.V. received earlier that day were "the most likely source of her fever." See id.[1]

A.V. exhibited no further seizure-like symptoms during the remainder of her time at the hospital. She also had no fever, and the electroencephalogram ("EEG") study of her brain activity was unremarkable. See Pet'rs' Ex. 3 pt. 2, at 57, 76. After about forty-two hours of observation, A.V. was prescribed diazepam for use as needed to treat acute seizure activity and was discharged with instructions to follow up with her pediatrician, Dr. Subramanian, in one to

[1] Because A.V.'s symptoms began within twenty-four hours of administration of vaccinations, hospital staff later contacted her pediatrician to recommend reporting A.V.'s febrile seizures as an adverse vaccine reaction to the Centers for Disease Control and Prevention. See Pet'rs' Ex. 3 pt. 2, at 75–76.

three days. See id. at 69 (admitting A.V. on April 21, 2015, 2:46 a.m.); id. at 78 (discharging A.V. on April 22, 2015, 8:23 p.m.).

As recommended, A.V. was examined by Dr. Subramanian on April 24, two days after her discharge from the hospital. See Pet'rs' Ex. 11, at 28. Dr. Subramanian listed epilepsy with complex seizures as her diagnosis. See id. at 29. She also noted a "possible diagnosis" of adverse effects from a bacterial vaccine. Id. Dr. Subramanian advised the Vinesars to have A.V. evaluated for complex seizures by a neurology specialist and instructed them to follow up in two months or as needed. See id.

B. A.V.'s Second Febrile Seizure

The following month, on May 14, 2015, A.V. presented for a pediatric neurology consult with Dr. Mohammad Ikramuddin. Pet'rs' Ex. 10, at 65, ECF No. 12-3. Dr. Ikkramuddin diagnosed A.V. with "[p]aroxysmal spells" and recommended that the Vinesars follow up with him in three months or earlier if necessary. Id. He also counseled the Vinesars on the "mechanism, known triggers, acute symptomatic measure[s], [and] chronic prophylaxis [of seizures], . . . [and on] the use of anti-seizure medication, including side effects, the need to monitor for side effects, seizure precautions[,] and reoccurrence risk." Id.

In late July 2015, two months after her visit with Dr. Ikramuddin, A.V. experienced a second seizure after a cold she had contracted a few days earlier caused her to develop a fever. See Pet'rs' Ex. 12 pt. 1, at 39, ECF No. 12-5 (July 26, 2015); Pet'rs' Ex. 11, at 25. At this point, A.V. was about ten months old. See Pet'rs' Ex. 12 pt. 1, at 27. A.V.'s mother administered diazepam after the seizure began, but it did not resolve A.V.'s symptoms. See id. EMS arrived, administered another sedative, and A.V.'s seizure activity stopped about ten minutes later. Id.

On route to the hospital and in the ED, A.V.'s temperature was recorded at 100.9° Fahrenheit. Id. at 27, 29. A.V. was admitted to the hospital and underwent an extensive diagnostic workup. See id. at 63–64 (EEG results); Pet'rs' Ex. 12 pt. 2, at 96–101, ECF No. 12-6 (complete blood count, comprehensive metabolic panel, respiratory viral panel, blood culture, urine culture, and chest x-ray results).

Notably, A.V. tested positive for parainfluenza virus type 3. Pet'rs' Ex. 12 pt. 2, at 99. Based on the test results, A.V.'s doctors concluded that the seizure she had experienced was caused by the fever brought on by her viral infection. See id. at 85. An EEG study of A.V.'s brain activity recorded the next day was "essentially unremarkable." Pet'rs' Ex. 12 pt. 1, at 63. A.V. was discharged that same day with a prescription for diazepam and instructions to follow up with Dr. Ikramuddin. Pet'rs' Ex. 12 pt. 2, at 86; see also Pet'rs' Ex. 12 pt. 1, at 9 (documenting A.V.'s discharge date and length of stay).

C. A.V.'s Third Febrile Seizure

A.V. had her follow-up exam with Dr. Ikramuddin on August 20, 2015. See Pet'rs' Ex. 10, at 54–56. He documented the details of A.V.'s recent seizure episode and discussed treating A.V.'s condition with anticonvulsant medication. See id. at 56. Given the possible side effects of the medication, however, A.V.'s parents declined this treatment option. Id.

Just under three months after this follow-up exam, on November 8, 2015, A.V. experienced a third seizure. See Pet'rs' Ex. 13, at 32, ECF No. 12-7. A.V.'s mother administered

diazepam, and A.V.'s seizure activity stopped one to two minutes thereafter. Id. EMS was called and once again transported A.V. to the ED. Id. In the ED, A.V.'s temperature was 102.6° Fahrenheit. Id. at 33 (recording A.V.'s temperature as 39.2° Celsius). Several hours later, A.V.'s initial labs were negative, her temperature had returned to normal, and she appeared "more awake and alert." Id. at 34.

Although the results of viral testing were still pending, the ED physician concluded that A.V. "likely has a virus, given sick contacts at home." Id. at 34. A.V. did not spend the night but was instead discharged, again with a prescription for diazepam and instructions to follow up with Drs. Subramanian and Ikramuddin within two to four days. Id. at 34–35.

The Vinesars met with Dr. Subramanian the next day. See Pet'rs' Ex. 11, at 21. She documented A.V.'s recent febrile seizure symptoms and advised the Vinesars to follow up with A.V.'s neurologist. Id.

D. A.V.'s Fourth Febrile Seizure

A.V.'s fourth seizure occurred about a month later, on December 5, 2015. See Pet'rs' Ex. 15, at 17, 37, ECF No. 13-2. On this occasion, A.V. had a temperature of 99.4° Fahrenheit and experienced a seizure about five minutes after she took Tylenol (acetaminophen) to reduce it. See id. Her mother administered diazepam one minute after the seizure-like symptoms began, and they ended about two minutes later. See id. at 17, 32, 37.

When A.V. presented in the ED after this episode, her temperature was 101.3° Fahrenheit. Id. at 20 (documenting A.V.'s arrival on Dec. 5, 2015, at 5:03 p.m.; recording A.V.'s temperature was 38.5° Celsius). A few hours later, however, A.V. was alert, eating normally, and no longer had a fever. Id. at 20–23. The ED discharged A.V., again with a prescription for diazepam and instructions to follow up with Drs. Subramanian and Ikramuddin within two to four days. Id. at 20, 22 (documenting A.V.'s discharge on Dec. 5, 2015, at 6:27 p.m.).

E. A.V.'s Seizures Continue; Seizure Disorder Diagnosed

On December 18, 2015, Dr. Subramanian conducted a follow-up exam of A.V. See Pet'rs' Ex. 11, at 19. Dr. Subramanian diagnosed A.V. with epilepsy. Id. at 19–20. Dr. Subramanian noted that A.V.'s fourth seizure was afebrile because her temperature just prior to the episode was only 99° Fahrenheit. See id. at 19. She advised the Vinesars to make an appointment with A.V.'s neurologist and encouraged them to start A.V. on prescription anti-seizure medication. Id. 19–20. The Vinesars rejected this suggestion and advised Dr. Subramanian that they wanted to pursue herbal therapy instead. Id. at 19.

In January 2016, the Vinesars presented to pediatric neurology specialist Dr. Nishant Shah for a re-evaluation of A.V.'s seizure disorder. See Pet'rs' Ex. 10, at 50 (Jan. 25, 2016). During the visit, Dr. Shah recommended that the Vinesars pursue magnetic resonance imaging ("MRI") of A.V.'s brain. See id. at 53. The Vinesars agreed to consider the recommendation. See id. Dr. Shah also opined that a forty-eight-hour video EEG "may be of value" if A.V. experiences a recurrence of seizure activity, especially if febrile. Id.

Later that year, A.V. experienced at least four more seizures with low or no fever present. See Pet'rs' Ex. 16, at 16–20, 27–29, ECF No. 13-3 (documenting seizure on Mar. 1, 2016);

Pet'rs' Ex. 17, at 16–17, 28–30, ECF No. 13-4 (documenting seizure on Sept. 12, 2023); Pet'rs' Ex. 10, at 20 (documenting seizures on Dec. 5, 2016, and Dec. 24, 2016).[2]

After the first two confirmed seizures in 2016, the Vinesars followed up with Dr. Shah. See Pet'rs' Ex. 10, at 41–45 (Mar. 22, 2016); id. at 31–35 (Sept. 22, 2016). During both visits, Dr. Shah reiterated his recommendations that the Vinesars obtain an MRI of A.V.'s brain and a forty-eight-hour video EEG. See Pet'rs' Ex. 10, at 34, 44. Nonetheless, as of the time A.V. experienced her third seizure in 2016, neither study had been performed. See id. at 34, 39. Dr. Shah also advised that given A.V.'s "recurrent seizures with no convincing fever or mild fever, and [her] subsequent diagnosis of epilepsy, [A.V.] will need to be on long-term antiseizure medic[ation]." See id. at 34. The Vinesars, however, remained "quite reluctant" to accept this recommendation. Id.

In November 2016, A.V. presented in Dr. Subramanian's clinic for her two-year well-child check-up. See Pet'rs' Ex. 11, at 14 (Nov. 4, 2016). In the notes from that check-up, Dr. Subramanian opined that A.V. continued to meet developmental milestones and noted that her seizure disorder was being followed by neurology. See id. at 14–15.

The next month, the Vinesars sought another opinion, this time with pediatric epilepsy specialist Dr. Sunila O'Connor. See id. at 69; see also Pet'rs' Ex. 37, at 4, ECF No. 41-1 (Dec. 13, 2016). Dr. O'Connor recommended obtaining an MRI of A.V.'s brain, a longer EEG, and certain metabolic studies to investigate the etiology of A.V.'s seizure disorder. See Pet'rs' Ex. 11, at 69. Based on A.V.'s history of prolonged seizures, Dr. O'Connor also recommended starting A.V. on antiepileptic medication after the diagnostic workup was complete. See id. Further—if neuroimaging, EEG, and metabolic studies were unremarkable—Dr. O'Connor felt that "genetic testing specifically looking at sodium channel abnormalities" would be prudent. See id.

The Vinesars rejected these suggestions and declined to pursue any radiological or laboratory studies or to start A.V. on medication. Id. Instead, the Vinesars told Dr. O'Connor that they intended to pursue "holistic methods" from "a person in their community who treats with multiple holistic medications." Id. Given that A.V.'s family did not want to pursue any of Dr. O'Connor's recommendations, Dr. O'Connor did not schedule a follow-up appointment and advised the Vinesars to pursue another opinion elsewhere or follow up with Dr. Shah as needed. See id.

The next month, the Vinesars brought A.V. to see Dr. Shah again. See Pet'rs' Ex. 10, at 20 (Jan. 16, 2017). Dr. Shah noted that A.V. had experienced febrile seizures on five occasions, that her first episode was prolonged when she "perhaps" had a mild fever, but that her more recent episodes occurred—or "quite likely" occurred—without fever. Id. at 24. Based on this recent history of recurrent seizures "with minimal or no fever," Dr. Shah concluded that A.V. had "epilepsy/seizure disorder" and again recommended anti-seizure medication. Id. Yet again,

[2] A.V. may have also had a seizure in July when she fell to the floor while playing on a couch, but it was never confirmed by her doctors. See Pet'rs' Ex. 18, at 18–19, ECF No. 13-5 (documenting A.V.'s possible seizure on July 19, 2016). In this instance, A.V. did not have a fever or lose consciousness, but her father reported she was unresponsive with her eyes rolling back and that she had difficulty standing up afterward. See id.

the family declined, and Dr. Shah informed them he could no longer participate in A.V.'s care if they did not follow his diagnostic and therapeutic recommendations. Id.

According to Ms. Vinesar, A.V.'s next seizures occurred in April and June 2017. Pet'rs' Ex. 1, at 3 (Apr. 1, June 7, and 23, 2017); see also Pet'rs' Ex. 11, at 61–66 (medical records regarding A.V.'s seizures on June 7 and 23, 2017). After the first seizure in June 2017, doctors started A.V. on Keppra (levetiracetam), an anticonvulsant. Pet'rs' Ex. 1, at 3.

On June 15, the Vinesars followed up with Dr. Subramanian. See Pet'rs' Ex. 11, at 12. During this visit, Ms. Vinesar reported that A.V. was receiving her anticonvulsant medication as prescribed but expressed concerns about the side effects of the medication. Id. Dr. Subramanian advised Ms. Vinesar about the benefits of anticonvulsant therapy and about how to avoid side effects. Id. She also recommended following up with neurology. Id.

Ms. Vinesar nonetheless discontinued the levetiracetam one week later because she believed A.V. was experiencing side effects. Pet'rs' Ex. 20, at 45.[3] The next day, June 23, 2017, the Vinesars brought A.V. to see Dr. Shah. See Pet'rs' Ex. 10, at 12.

At the outset of her visit with Dr. Shah, A.V. experienced "a prolonged seizure lasting at least [fifteen] minutes" and was transferred to the pediatric intensive care unit ("ICU"). Id. After examining A.V. in the ICU, the pediatric intensivist opined that A.V.'s seizure was "likely due to medical noncompliance" rather than "infectious etiology at this time." Pet'rs' Ex. 20, at 50.

While in the hospital, the Vinesars consented to an MRI of A.V.'s brain and a brief EEG, but the results from both studies were unremarkable. See id. at 25, 92. Hospitalists also transitioned A.V. off levetiracetam and started another anticonvulsant, Trileptal (oxcarbazepine), to manage her seizures. Id. at 55.

According to Ms. Vinesar, A.V. had ten more seizures in the two months that followed her discharge from the hospital. See Pet'rs' Ex. 1, at 3 (July 1, 6, 11, 16, 26, Aug. 4, 6, 11, and 23, 2017); see also Pet'rs' Ex. 10, at 2 (July 6, 2017); Pet'rs' Ex. 22, at 19–20 (July 1, 2017); Pet'rs' Ex. 23, 19–22 (Aug. 23, 2017); Pet'rs' Ex. 34, at 3 ("Patient had been having seizures every 5–10 days leading to the events of [August 23, 2017].").[4]

In late August, EMS brought A.V. to the ED during a seizure that lasted over half an hour. See Pet'rs' Ex. 23, at 17, 20 (noting that A.V.'s seizure activity started twenty minutes before EMS arrival at 8:32 PM and did not stop until Ativan (lorazepam) was administered upon arrival in the ED at 8:46 PM). While in the ED this time, Ms. Vinesar told A.V.'s doctor that she had taken A.V. off the oxcarbazepine against Dr. Shah's advice. See id. at 20.

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[3] Petitioners' Exhibit 20 is not accessible on the electronic docket. This exhibit is stored on a compact disc that Petitioners filed with the Clerk of the Court on June 25, 2018. See Pet'rs' Notice of Intent to File at 1, ECF No. 18.

[4] Petitioners' Exhibits 22–23 and 34 are not accessible on the electronic docket. These exhibits are stored on a compact disc that Petitioners filed with the Clerk of the Court on June 25, 2018. See Pet'rs' Notice of Intent to File at 1.

The next day, A.V. underwent a "24-hour long-term video EEG monitoring study." Pet'rs' Ex. 11, at 54–55 (Aug. 24–25, 2017). According to the neurology specialist at the University of Chicago who interpreted the results, Dr. Charles Marcuccilli, A.V.'s brain activity demonstrated "focal sites of cerebral hyperexcitability," possibly associated "with partial seizures/epilepsy," and "diffuse cerebral dysfunction" potentially caused by "structural or vascular abnormalities, toxic, metabolic conditions, hydrocephalus or postictal conditions." Id. at 55.

A few weeks later, the Vinesars brought A.V. to see Dr. Subramanian for her three-year well-child check-up. See id. at 7 (Sept. 15, 2017). At this visit, Dr. Subramanian noted that the University of Chicago now followed A.V.'s seizure disorder, A.V. was taking levetiracetam, and she continued to meet developmental milestones. See id.

F. Genetic Testing and Dravet Syndrome Diagnosis

In October, after yet another series of seizures, see Pet'rs' Ex. 1, at 3 (Sept. 8, 23, 27, Oct. 21, and 28, 2017), Dr. Marcuccilli ordered neurogenetic testing, see Pet'rs' Ex. 4, at 2, ECF No. 1-9. The testing included sequencing and deletion/duplication analysis on a panel of eighty-seven genes. Id. The results indicated that A.V. has "a novel pathogenic variant and a variant of uncertain significance in the SCN1A gene." Id.

According to the report, A.V.'s variant of unknown significance was predicted to damage protein structure or function. Id. at 4. However, the report stated "[b]ased on the currently available information, it is unclear whether this variant is a pathogenic variant or a rare benign variant." Id. A.V.'s pathogenic variant was deemed consistent with the "diagnosis of a SCN1A-related disorder" as it "is predicted to cause loss of normal protein function either through protein truncation or nonsense-mediated mRNA decay." Id. at 2–3. Additionally, the report notes that 70–80% of Dravet syndrome, 20–24% of early-onset cryptic epilepsy, and 5–10% of genetic epilepsy with febrile seizures plus ("GEFS+") are associated with mutations in the SCN1A gene. See id. at 6.[5]

In April 2018, the Vinesars brought A.V. to the neurology clinic at the University of Chicago for follow-up. See Pet'rs' Ex. 34, at 385 (Apr. 4, 2018). The neurologist's impression was that A.V. had Dravet syndrome due to her SCN1A gene mutation. See id. at 390. By this point, A.V.'s doctors had swapped levetiracetam for ONFI (clobazam), a sedative medication used to treat certain types of seizures. See id. at 389. But because the Vinesars felt the new medication was causing A.V. to experience abdominal pain and somnolence, the family sought to initiate a ketogenic diet to treat A.V.'s seizures in lieu of pharmacotherapy. Id. at 390. At the

[5] A.V. had repeat genetic testing performed at a different laboratory in June 2018. See Pet'rs' Ex. 39, at 1, ECF No. 42-1. This test provided "[s]equence analysis and deletion/duplication testing" of 133 genes. Id. Repeat testing identified the same "[p]athogenic variant" and "[v]ariant of [u]ncertain [s]ignificance" that the first test identified in A.V.'s SCN1A gene. Compare id. with Pet'rs' Ex. 4, at 2. Likewise, the report indicates that "[t]he SCN1A gene is associated with a spectrum of autosomal dominant seizure disorders ranging from simple febrile seizures and genetic epilepsy with febrile seizures plus (GEFS+) to Dravet syndrome and intractable childhood epilepsy with generalized tonic-clonic seizures." Pet'rs' Ex. 39, at 1 (citations omitted).

end of the visit, the neurologist lowered A.V.'s dose of clobazam and referred her to the ketogenic diet clinic. See id. Additionally, since Ms. Vinesar continued to express doubt about A.V.'s diagnosis, the doctor advised the Vinesars to seek a third opinion at a nearby Dravet syndrome specialty clinic. See id.

Dr. Marcucilli examined A.V. once again in June 2018. See Pet'rs' Ex. 41, at 46, ECF No. 42-3 (June 21, 2018). During this visit, the Vinesars updated Dr. Marcucilli on A.V.'s medical history. Id. They shared that "[t]he longest [A.V.] has gone seizure free [was] 39 days." Id. Nevertheless, despite "significant drowsiness" and "some slurred speech," A.V. was "otherwise developing normally." Id. Dr. Marcucilli then reviewed A.V.'s medical history of prolonged seizures, her genetic profile, and the results of four EEG studies. Id. at 48–49. Based on this information, Dr. Marcucilli diagnosed A.V. with "Dravet [s]yndrome with intractable epilepsy secondary to an SCN1A mutation." Id.

G. A.V.'s Subsequent Medical History

A.V. continued to experience two to three seizures per month over the next few years. See Pet'rs' Ex. 147, at 2, ECF No. 115-4 (Nov. 11, 2021). Nevertheless, Ms. Vinesar reported at A.V.'s six-year well-child checkup that A.V. was being homeschooled and "doing well with learning, speech[,] and development" except for "periods of set back following a seizure episode." See id. at 5 (Mar. 30, 2021). As of November 2021, A.V. had a "[s]peech problem" and was taking antiseizure medication for "Dravet syndrome, intractable, with status epilepticus." See Pet'rs' Ex. 148, at 1, ECF No. 115-5 (Nov. 17, 2021).

II. Procedural Background

A. Proceedings Before the Special Master

On March 23, 2018, Petitioners filed a petition for compensation under the National Vaccine Injury Compensation Program, 42 U.S.C. §§ 300aa-1 to -34, on A.V.'s behalf. See Petition at 1, ECF No. 1. In their petition, they alleged that "covered vaccinations" administered to A.V. on April 20, 2015, caused a seizure disorder that first presented "within half a day of the vaccination and continues to afflict [A.V.]." Id. at 1.

Along with their petition, the Vinesars attached A.V.'s medical records and a letter from their expert, Dr. Marcel Kinsbourne. See Pet'rs' Ex. 2, at 2, ECF No. 1-3. In that letter, Dr. Kinsbourne opined that recent progress in the understanding of SCN1A mutations have undermined several assumptions that special masters relied on in the past when denying compensation to children with SCN1A mutations. Id. at 1–2; see also Oliver v. Sec'y of Health & Hum. Servs., No. 10-394V, 2017 WL 747846, at *25–26 (Fed. Cl. Spec. Mstr. Feb. 1, 2017) (noting compensation has been denied in at least sixteen cases involving children with SCN1A mutations), review denied, 133 Fed. Cl. 341 (2017), aff'd 900 F.3d 1357 (Fed. Cir. 2018).

The Secretary filed his Vaccine Rule 4(c) report on December 19, 2018. See Resp't's Rep. at 1–2, 19, ECF No. 29; see also RCFC App. B, Vaccine Rule 4(c). He recommended the denial of compensation, contending that Petitioners had "failed to proffer a medical opinion or theory sufficient to establish a logical cause and effect relationship between [A.V.'s] vaccines and her condition." Resp't's Rep. at 19. Specifically, the Secretary observed that A.V. possesses a known pathogenic variant "consistent with the diagnosis of an SCN1A-related disorder" and

that "[A.V's] own treating doctors have attributed [her] seizure disorder to a mutation in her SCN1A gene." See id. at 17.

Along with his recommendation, the Secretary submitted an expert report by Dr. Gerald Raymond, a pediatric neurologist and clinical geneticist. See generally Resp't's Ex. A, ECF No. 30-1. Dr. Raymond responded to Dr. Kinsbourne's opinion and the medical literature on which he relied. See id. at 4–6. According to Dr. Raymond, the mutation in A.V.'s SCN1A gene was "the sole cause" of her seizure disorder and "[i]t was not caused nor exacerbated by any of the immunizations that she received." See id. at 6.

The Vinesars subsequently filed additional medical records, Pet'rs' Exs. 35–41, ECF Nos. 38, 41–42, and two supplemental reports by Dr. Kinsbourne, Pet'rs' Exs. 45–46, ECF Nos. 51, 55. They also submitted expert reports from Dr. Mark McNulty, a statistician, Pet'rs' Ex. 81, ECF No. 64-1, and Dr. Richard Boles, a pediatrician and medical geneticist, Pet'rs' Exs. 82, 153, ECF Nos. 68-1, 121-2. In addition, they further supplemented the record by filing additional medical literature. See Pet'rs' Exs. 110–121, 124–127, ECF Nos. 92–94.

In January 2022, Petitioners filed a motion for a ruling on the record, Pet'rs' Mot. for J. on Admin. R., ECF No. 124 [hereinafter "Pet'rs' MJAR"], to which the Secretary responded on March 25, 2022, Resp't's Resp. to MJAR, ECF No. 127. On January 18, 2023, the Special Master held oral argument on several questions raised by the parties' briefs. See generally Oral Arg. Tr., ECF No. 135.

The Special Master denied Petitioners' motion for a ruling on the record on July 28, 2023. See Dec. at 1. In his view, Petitioners failed to prove the DTaP vaccine that A.V. received either caused or significantly aggravated her Dravet syndrome. See id. at 51–52. He also found, in the alternative, that the Secretary proved that a factor unrelated to the vaccine—namely her SCN1A variant—was the sole reason why she developed Dravet syndrome. See id. at 74.

B. The Present Motion for Review

Petitioners filed their motion for review of the Special Master's decision with the Court on August 14, 2023, and the Secretary filed a response urging the Court to affirm the Special Master's decision. See generally Pet'rs' Mot. for Rev., ECF No. 138 [hereinafter "Pet'rs' Mot. for Rev. I"]; Respt's Resp. to Pet'rs' Mot. for Rev., ECF No. 141 [hereinafter "Gov't's Resp. I"].

Petitioners' motion did not comply with the requirements of the Vaccine Rules of the United States Court of Federal Claims. The Court therefore ordered Petitioners to file a corrected motion for review and granted the Secretary leave to file a supplemental response to the corrected motion. See Order, Sept. 26, 2023, ECF No. 142. Shortly thereafter, Petitioners timely filed their "corrected" motion, and the Secretary subsequently supplemented his initial response. See generally Pet'rs' Corrected Mot. for Rev., Oct. 1, 2023, ECF No. 143 [hereinafter "Mot. for Rev. II"]; Respt's Resp. to Pet'rs' Corrected Mot. for Rev., Oct. 5, 2023, ECF No. 144 [hereinafter "Gov't's Resp. II"].

The Court has considered the arguments in Petitioners' "corrected" motion for review and concludes that Petitioners have failed to demonstrate that the Special Master's decision was arbitrary, capricious, an abuse of discretion, or contrary to law. The Motion for Review is therefore denied, and the Special Master's decision is sustained.

DISCUSSION

I. Jurisdiction

Congress established the National Vaccine Injury Compensation Program in 1986 to provide a no-fault compensation system for vaccine-related injuries and deaths. Figueroa v. Sec'y of Health & Hum. Servs., 715 F.3d 1314, 1316–17 (Fed. Cir. 2013); see also 42 U.S.C. §§ 300aa–10 to –34. The Act is "[r]emedial legislation" which "should be construed in a manner that effectuates its underlying spirit and purpose." Figueroa, 715 F.3d at 1317 (alteration in original) (citing Cloer v. Sec'y of Health & Hum. Servs., 675 F.3d 1358, 1362 (Fed. Cir. 2012)).

A petition seeking compensation under the Vaccine Act must be filed in the Court of Federal Claims, after which the Clerk of the Court forwards it to the Office of Special Masters for assignment. 42 U.S.C. § 300aa–11(a)(1). The special master to whom the petition is assigned "issue[s] decision on such petition with respect to whether compensation is to be provided under the [Vaccine Act] and the amount of such compensation." Id. § 300aa–12(d)(3)(A).

The Vaccine Act grants the Court of Federal Claims jurisdiction to review the decisions of special masters (subject to further review in the Federal Circuit). Mahaffey v. Sec'y of Health & Hum. Servs., 368 F.3d 1378, 1383 (Fed. Cir. 2004) (citing 42 U.S.C. § 300aa–12(d)(3)(A)). On review, the Court may:

> (1) uphold the findings of fact and conclusions of law of the special master and sustain the special master's decision[;]
>
> (2) set aside any findings of fact or conclusion of law of the special master found to be arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law and issue its own findings of fact and conclusions of law[;] or
>
> (3) remand the petition to the special master for further action in accordance with the court's direction.

42 U.S.C. § 300aa–12(e)(2); see also RCFC App. B, Vaccine Rule 27.

II. Standard of Review

The Court reviews a special master's legal determinations de novo, applying the "not in accordance with law" standard. Moberly v. Sec'y of Health & Hum. Servs., 592 F.3d 1315, 1321 (Fed. Cir. 2010); Althen v. Sec'y of Health & Hum. Servs., 418 F.3d 1274, 1278–79 (Fed. Cir. 2005); see also Carson v. Sec'y of Health & Hum. Servs., 727 F.3d 1365, 1368 (Fed. Cir. 2013) (instructing the reviewing court to "give no deference to the . . . Special Master's determinations of law"). Review of a special master's factual determinations, on the other hand, is circumscribed. Such determinations will be set aside only if they are arbitrary, capricious, and/or reflect an abuse of discretion. Moberly, 592 F.3d at 1321.

The standard of review of a special master's factual determinations is a "uniquely deferential" one. Milik v. Sec'y of Health & Hum. Servs., 822 F.3d 1367, 1376 (Fed. Cir. 2016) (quoting Hodges v. Sec'y of Health & Hum. Servs., 9 F.3d 958, 961 (Fed. Cir. 1993)). The Court does not reweigh the evidence nor examine its probative value or the credibility of the witnesses; those "are all matters within the purview of the fact finder." Porter v. Sec'y of Health & Hum. Servs., 663 F.3d 1242, 1249 (Fed. Cir. 2011) (citing Broekelschen v. Sec'y of Health & Hum.

Servs., 618 F.3d 1339, 1349 (Fed. Cir. 2010)). Therefore, if a special master "'has considered the relevant evidence of record, drawn plausible inferences and articulated a rational basis for the decision,' then reversible error is 'extremely difficult to demonstrate.'" Milik, 822 F.3d at 1376 (quoting Hines v. Sec'y of Health & Hum. Servs., 940 F.2d 1518, 1528 (Fed. Cir. 1991)).

III. The Petitioners' Burden of Proof

To make a prima facie case of entitlement to compensation under the Vaccine Act, a petitioner must prove by preponderant evidence that the "illness, disability, injury, or condition" at issue was caused—or significantly aggravated—by a vaccine. See 42 U.S.C. §§ 300aa–11(c)(1), –13(a)(1). There are two avenues by which a petitioner may establish causation: the on-table claim and the off-table claim. Broekelschen, 618 F.3d at 1341–42 (citing 42 U.S.C. § 300aa-11(c)(1)(C)(i); Andreu ex rel. Andreu v. Sec'y of Health & Hum. Servs., 569 F.3d 1367 (Fed. Cir. 2009)).

In an on-table claim, causation is presumed if the petitioner can show (1) that he or she received a vaccination listed in the Vaccine Injury Table, 42 U.S.C. § 300aa–14, as revised by 42 C.F.R. § 100.3(a), and (2) that he or she suffered an injury associated with that vaccine within the period of time prescribed by the table. See Andreu, 569 F.3d at 1374 (citing 42 U.S.C. § 300aa–11(c)(1)(C)(i)).

Petitioners' claim that the third dose of the DTaP vaccine administered to A.V. caused the development or worsening of her Dravet syndrome does not allege an on-table injury. See 42 C.F.R. § 100.3(a). There is no presumption of causation for off-table claims. For off-table claims, the petitioner must prove by preponderant evidence that any claimed injury was either caused or significantly aggravated by a vaccine. See W.C. v. Sec'y of Health & Hum. Servs., 704 F.3d 1352, 1356–57 (Fed. Cir. 2013) (quoting Althen, 418 F.3d at 1278; Loving v. Sec'y of Health & Hum. Servs., 86 Fed. Cl. 135, 144 (2009)); see also Sharpe v. Sec'y of Health & Hum. Servs., 964 F.3d 1072, 1078 (Fed. Cir. 2020) (citing 42 U.S.C. § 300aa–11(c)(1)(C); Whitecotton ex rel. Whitecotton v. Sec'y of Health & Hum. Servs., 81 F.3d 1099, 1102–03 (Fed. Cir. 1996)).

To prove that a vaccine caused an injury, petitioners must establish: (1) a "medical theory causally connecting the vaccination and the injury"; (2) a "logical sequence of cause and effect showing that the vaccination was the reason for the injury"; and (3) a "proximate temporal relationship between vaccination and injury." Althen, 418 F.3d at 1278.

Petitioners asserting significant aggravation claims must produce preponderant evidence showing: (1) the vaccine recipient's "condition prior to administration of the vaccine"; (2) their "current condition (or the condition following the vaccination if that is also pertinent)"; and (3) whether their "current condition constitutes a 'significant aggravation' of [their] condition prior to vaccination." W.C., 704 F.3d at 1357 (quoting Loving, 86 Fed. Cl. at 144).

If these elements are proven, then petitioners must make a showing similar to the one required to prove causation under Althen. They must demonstrate by a preponderance of evidence: (1) a "medical theory causally connecting such a significantly worsened condition to the vaccination"; (2) a "logical sequence of cause and effect showing that the vaccination was the reason for the significant aggravation"; and (3) a "proximate temporal relationship between the vaccination and the significant aggravation." Id.

A failure to establish any one of the required elements set forth in Althen or Loving, "is necessarily fatal to a petitioner's case." See Hodge ex rel. Elson v. Sec'y of Health & Hum. Servs., 168 Fed. Cl. 117, 124 (2023). On the other hand, if a petitioner has satisfied the criteria required to show causation-in-fact under Althen, or significant aggravation under Loving, he or she is entitled to compensation "unless the government can show by a preponderance of the evidence that the injury is due to factors unrelated to the vaccine." See Broekelschen, 618 F.3d at 1342 (citing Doe v. Sec'y of Health & Hum. Servs., 601 F.3d 1349, 1351 (Fed. Cir. 2010)); see also 42 U.S.C. § 300aa-13(a)(1)(B).

IV. The Expert Opinions

The parties submitted dueling expert opinion reports for the Special Master's consideration. Petitioners' experts included Dr. Marcel Kinsbourne, a pediatric neurologist, Dr. Mark McNulty, a statistician, and Dr. Richard Boles, a pediatrician and medical geneticist. See generally Pet'rs' Exs. 2, 45–46, 81–82, 153. The Secretary's expert was Dr. Gerald Raymond, a pediatric neurologist and clinical geneticist. See generally Resp't's Exs. A, C–D.

The Court notes for context that Drs. Raymond, Kinsbourne, and Boles have frequently appeared as experts in cases involving claims that a vaccine caused a child with the SCN1A genetic defect to develop Dravet syndrome. See Dec. at 2–32 (summarizing cases). Based in part on findings that Dr. Raymond's qualifications were superior to those of the other experts in the cases, the special masters reviewing the claims in every one of these cases have credited his opinion that a defect in the SCN1A gene, and not a vaccine, caused the vaccine recipient to develop Dravet syndrome. See id.

In his first report, Dr. Kinsbourne cited a study described by Cetica et al., which he interpreted as showing that febrile seizures (whether or not caused by the DTaP vaccine) increase the chances that a child with the genetic mutation will develop Dravet syndrome. See Pet'rs' Ex. 2, at 1 (citing Valentina Cetica et al., Clinical and Genetic Factors Predicting Dravet Syndrome in Infants with SCN1A Mutations, 88 Neurology 1037 (2017)). Further, he stated, when the DTaP vaccine triggers Dravet syndrome, it accelerates the onset of the disorder by some two months. Id. Dr. Kinsbourne also cited Dutton et al., which studied mice with the mutation and found that "early-life [febrile seizures] resulted in lower latencies to induced seizures, increased [the] severity of spontaneous seizures, hyperactivity, and impairments in social behavior and recognition memory during adulthood." Id. (quoting Stacey B.B. Dutton et al., Early-Life Febrile Seizures Worsen Adult Phenotypes in SCN1A Mutants, 293 Experimental Neurology 159, 159 (2017)).

Dr. Raymond prepared a report expressing disagreement with Dr. Kinsbourne's opinion and his interpretation of the medical literature he cited in support of that opinion. See Resp't's Ex. A, at 4–6. He specifically addressed and rejected Dr. Kinsbourne's interpretation of, and reliance on, the Cetica and Dutton articles. See id. at 5. He stated that it was his view "to a reasonable degree of medical certainty" that a mutation in A.V.'s SCN1A gene "is the sole cause of her epilepsy condition," and that "[i]t was not caused nor exacerbated by any of the immunizations that she received." See id. at 6.

Dr. Raymond stated that his opinion—that a genetic mutation and not a vaccine causes Dravet syndrome—was supported by a study on early seizure events secondary to vaccination in Dravet syndrome by McIntosh et al. See id. at 5–6. Dr. Raymond noted that the researchers for

that article found that "although vaccination might sometimes seem to trigger the onset of Dravet syndrome," there was no evidence that "vaccination itself affect[ed] the severity of the disorder." See id. at 6. He also stated that "[t]here is no evidence that the timing of the first seizure in any way alters the tragic course of this genetic disorder." Id. Children with Dravet syndrome, he opined, typically have the onset of seizures in their first year of life and those seizures subsequently "escalate in type and severity." Id.

Dr. Kinsbourne provided two supplemental reports in which he responded to Dr. Raymond's opinion. See generally Pet'rs' Exs. 45–46. In the first report, he reviewed A.V.'s medical history and described what he understood to be the mechanism by which the DTaP vaccination that A.V. received caused, or at least exacerbated, her seizure disorder. See Pet'rs' Ex. 45, at 7–14, ECF No. 51-1. Dr. Kinsbourne disagreed with Dr. Raymond's conclusion that A.V.'s SCN1A mutation was the sole cause of her Dravet syndrome. See id. at 13. He also opined that Dr. Raymond's opinions were contradicted by the medical literature Dr. Kinsbourne summarized in his supplemental report. See id. at 12–13. He concluded that "[a]bsent the vaccinations [A.V. received,] a later onset, if any, of a milder seizure disorder would have been expected." Id. at 14.

In his second supplemental report, Dr. Kinsbourne summarized a recent article by Salgueria-Pereira et al. and discussed how the findings in the article were relevant to A.V.'s clinical condition. See Pet'rs' Ex. 46, at 1–2, ECF No. 55. He observed that Salgueria-Pereira found that "seizures are important contributors to the development of severe phenotypes in carriers of SCN1A variants" and that therapeutic approaches "should aim [to] . . . reduce[] their occurrence as much as possible." See id. at 2. Applying these findings to A.V.'s case, Dr. Kinsbourne opined that it was "more likely than not" that A.V.'s condition would be "significantly more benign had . . . routine vaccinations not initiated or triggered her . . . seizure disorder." Id. at 2.

As noted, Dr. McNulty, a statistician, also submitted a report for Petitioners. See generally Pet'rs' Ex. 81. He discussed the McIntosh article that Dr. Raymond cited and noted several flaws in the investigators' statistical analyses. See id. at 2. Dr. McNulty asserted that the investigators "incorrectly implie[d] that [DTaP] vaccinations have no long-term impacts on outcomes." Id. (footnote omitted). In his view, "the data in this study are not strong enough to reach meaningful conclusions regarding the impacts of vaccination due to the small sample sizes . . . analyzed." Id.

Petitioners' third expert, Dr. Boles, submitted a report discussing several articles that addressed SCN1A mutations and Dravet syndrome. See generally Pet'rs' Ex. 82. Dr. Boles opined that "SCN1A mutations are associated with a wide range of neurological disease phenotypes" and that environmental factors, such as fever, contribute to greater disease severity. See Pet'rs' Ex. 82, at 4, 6–9. Accordingly, it was Dr. Boles' opinion that "vaccinations significantly aggravated [A.V.'s] epilepsy, . . . resulting in the early []onset of seizures and a worsened clinical outcome" and that, "if she had not been vaccinated, . . . her outcome would have been better than it is today, and projected to be in the future." See id. at 13.

In response to the foregoing, the Secretary filed another report by Dr. Raymond. See generally Resp't's' Ex. C, ECF No. 77. Dr. Raymond discussed the reports of Drs. Kinsbourne, McNulty, and Boles, and provided citations to medical literature that he said contradicted their opinions. See id. at 3–15. Among other things, he challenged Dr. McNulty's critique of the

statement in the McIntosh article that "it is unknown whether [patients with Dravet syndrome that first presented less than one day after vaccination] would have had milder outcomes had they not been vaccinated at all." Id. at 10 (citing Pet'rs' Ex. 81, at 5). Dr. Raymond agreed that "[i]t is very clear from the understanding of the biology of the variants in SCN1A . . . that there is a spectrum of outcomes." Id. However, he noted, "the severe end of that spectrum . . . may present with medically refractory seizures, intellectual disability, ataxia, sleep disturbances, and other manifestations." Id. He added that a recent study of 504 patients with SCN1A variants by Brunklaus et al. demonstrated that 99.6% of the patients with protein truncation variants—like the variant A.V. has—had Dravet syndrome. See id. (citing Andrea Brunklaus et al., Biological Concepts in Human Sodium Channel Epilepsies and Their Relevance in Clinical Practice, 61 Epilepsia 387 (2020)). According to Dr. Raymond, these results illustrated "how knowledge of the genetic variant and its action on the particular channel produced direct clinical information." Id. He again opined, "to a reasonable degree of medical certainty," that A.V.'s SCN1A mutation "[wa]s the sole cause of her epilepsy disorder" and none of the immunizations that she received caused or exacerbated it. Id. at 15.

V. The Special Master's Decision

As reflected in his decision, the Special Master reviewed A.V.'s medical records and the reports of both parties' experts. He also reviewed the medical literature on which the experts relied. Applying the Althen and Loving frameworks, he concluded that Petitioners failed to establish that A.V.'s seizure disorder was caused or significantly aggravated by the DTaP vaccination she received in April 2015. See Dec. at 44–52. Therefore, he found, Petitioners had not established a prima facie case of a vaccine-related injury. See id. at 51–52

The Special Master's findings rest on two independent grounds: (1) that Petitioners did not provide a reliable medical theory that explained how the DTaP vaccine "can harm a recipient, either by causing . . . or by aggravating a seizure disorder" (Althen prong 1; Loving prong 4); and (2) that they had also not shown that the vaccination A.V. received "was the logical reason for either the development . . . or worsening of [her] seizure disorder" (Althen prong 2; Loving prong 5). Id. at 51–52.

Finally, the Special Master concluded, even if Petitioners had proven a prima facie case of a vaccine-related injury, the Secretary had established by preponderant evidence that a factor unrelated to a vaccination—i.e., an SCN1A gene mutation—was the sole cause of A.V.'s seizure disorder. Id. at 52–74. Therefore, he ruled, A.V. was not entitled to compensation under the Vaccine Act. Id. at 76.

V. Petitioners' Objections to the Special Master's Decision

Under Vaccine Rule 24, a motion for review of the decision of a special master must include a memorandum of "numbered objections," which "fully and specifically state and support each objection . . . [with] citations to the record" and "set forth any legal arguments the party desires to present to the reviewing judge." See RCFC App. B, Vaccine Rule 24(a), (b)(1)–(2). As noted above, the first motion for review that Petitioners filed did not meet these requirements. It consisted largely of conclusory statements, did not contain numbered objections to the Special Master's decision, and did not support each of Petitioners' objections with citations to the record and controlling law. See Vaccine Rule 24(b); see generally Pet'rs' Mot. for Rev. I.

At the Court's direction, Petitioners filed a corrected motion for review. The corrected motion includes three numbered objections to the Special Master's decision. See Pet'rs' Mot. for Rev. II, at 1–2. Beyond that, it was not much of an improvement, if at all, over the original motion. Petitioners' corrected motion does not provide specific citations to the record or the Special Master's decision for the vast majority of the assertions it contains, leaving the Court to guess their basis. See generally id. It also contains misspellings, odd capitalization, words that run together, and multiple difficult—if not impossible—passages to follow. See, e.g., id. at 1–2, 6, 8, 10.

As best the Court can understand them, Petitioners' first two objections to the Special Master's decision challenge the factual determinations that underly his conclusion that Petitioners failed to establish a prima facie showing of causation under Althen and Loving. They contend, for example, that the Special Master erroneously found that the seizure A.V. suffered shortly after receiving the DTaP vaccine was a "one off" that caused no lasting harm. See id. at 1. This was error, according to Petitioners, because under the diagnostic criteria for Dravet syndrome, EEG studies in children with Dravet syndrome are initially normal. See id. Second, Petitioners object to the Special Master's finding that there was insufficient support for their contention that A.V.'s vaccine-induced seizure aggravated her seizure disorder by causing its early onset, which in turn had the effect of increasing its severity. See id.

Petitioners' third objection to the Special Master's decision appears to be a legal one. The Special Master ruled that—even assuming Petitioners had established a prima facie case of either causation or significant aggravation under Althen or Loving—they would nonetheless not be entitled to compensation because the Secretary has shown by preponderant evidence that a factor unrelated to the vaccine—namely A.V.'s genetic mutation—was the sole cause of her Dravet syndrome. See Dec. at 74; see also Broekelschen, 618 F.3d at 1342 (citing Doe, 601 F.3d at 1351 (explaining that once a petitioner has demonstrated causation or significant aggravation, he or she "is entitled to compensation unless the government can show . . . the injury is due to factors unrelated to the vaccine")); 42 U.S.C. § 300aa-13(a)(1)(B). Petitioners contend that the Special Master's determination that the Secretary met his burden of showing that factors unrelated to the vaccine caused A.V.'s Dravet syndrome conflicts with the court of appeals' decision in Sharpe v. Sec'y of Health & Hum. Servs., 964 F.3d 1072 (Fed Cir. 2020). See Pet'rs' Mot. for Rev. II at 2.

Petitioners have a steep hill to climb to demonstrate reversible error based on their first two objections to the Special Master's decision. As noted above, the scope of judicial review of the Special Master's factual findings is exceptionally narrow and deferential. The Court does not reweigh the evidence. Nor does it second-guess the Special Master's assessment of the credibility of expert witnesses. Its role is instead to ensure that the Special Master reviewed all of the relevant evidence, drew plausible inferences, provided an adequate explanation for his conclusions, and made factual findings that are not arbitrary and capricious or an abuse of discretion.

Moreover, unless Petitioners have satisfied their burden of establishing causation under Althen or significant aggravation under Loving, the burden to prove that some other factor (e.g., an SCN1A gene mutation) was the sole cause of A.V.'s injury does not shift to the Secretary. LaLonde v. Sec'y of Health & Hum. Servs., 746 F.3d 1334, 1340 (Fed. Cir. 2014) (citing Althen, 418 F.3d at 1278). Therefore, to the extent that Petitioners do not prevail as to the fact-based

challenges they present in their first two objections, it is unnecessary for the Court to address their third objection.

For the reasons set forth below, the Court concludes that the Special Master's findings that Petitioners did not satisfy their burden of establishing causation under Althen or significant aggravation under Loving are supported by the relevant evidence of record. Their motion for review must therefore be denied.

A. The Special Master's Finding that Petitioners Failed to Supply a Sound and Reliable Medical Theory Explaining How the DTaP Vaccine Could Have Caused A.V. to Develop a Seizure Disorder (Althen Prong 1)

As discussed above, to make a prima facie case of a vaccine-related injury under Althen, a petitioner must set forth a medical theory explaining how the vaccine caused the injury allegedly suffered. The theory of causation need not be "medically or scientifically certain," but it must be informed by a "sound and reliable medical or scientific explanation." See Knudsen ex rel. Knudsen v. Sec'y of Health & Hum. Servs., 35 F.3d 543, 548–49 (Fed. Cir. 1994) (quoting Bunting v. Sec'y of Health & Hum. Servs., 931 F.2d 867, 873 (Fed. Cir. 1991)); see also Boatmon v. Sec'y of Health & Hum. Servs., 941 F.3d 1351, 1360 (Fed. Cir. 2019); W.C., 704 F.3d at 1356 ("[T]he petitioner must do more than demonstrate a 'plausible' or 'possible' causal link between the vaccination and the injury; [they] must prove [their] case by a preponderance of the evidence." (quoting Moberly, 592 F.3d at 1322)).

In this case, Petitioners have argued that the DTaP vaccine can cause a fever and that fevers can cause seizures. Dec. at 45; see also Pet'rs' MJAR at 4–5; Oral Arg. Tr. at 9–10, 58; Pet. at 5. This contention is supported by the medical literature and was endorsed by both parties' experts, as well as the Special Master. See Dec. at 45–49. But the dispute under Althen prong 1 is not about whether the vaccine could have caused A.V.'s first seizure. It concerns whether Petitioners supplied a reliable medical or scientific theory to explain how the vaccine could have caused A.V.'s seizure disorder. And based on the medical literature the Special Master examined, as well as the opinions of Dr. Raymond, he found that Petitioners had not. Id. at 49.

The Special Master began his discussion of the medical literature with the earliest article Petitioners cited: M.H. Bellman et al., Infantile Spasms and Pertussis Immunisation, 321 Lancet 1031 (1983). The authors of that article studied the diphtheria-tetanus-whole-cell-pertussis ("DTwP") vaccine. See Dec. at 46. Petitioners did not file the article as an exhibit and their experts did not cite it. Nonetheless, the Special Master reviewed and discussed it. He credited the opinion of the Secretary's expert, Dr. Raymond, that the Bellman article was inapposite because it studied persons who were administered a different vaccine and who experienced a specific subtype of seizures that does not share any clinical characteristics with Dravet syndrome. See id. (citing Resp't's Ex. D, at 1–2, ECF No. 128-1 (explaining that A.V. "did not develop infantile spasms nor did she receive [the DTwP] vaccine")).

The Special Master was also unpersuaded that the other articles Petitioners and their experts cited provided a sound and reliable medical theory tying the DTaP vaccine to the development of seizure disorders like Dravet syndrome. At best, he found, the other articles showed that the vaccine can cause fevers, which in turn cause seizures, which is, as noted above, a point that is not in dispute. See id. at 46–48.

The Conrad & Jenson article, for example, examined data from the Centers for Disease Control & Prevention and the American Academy of Pediatrics Committee on Infectious Disease. See id. at 46. Based on that data, the authors concluded that "DTaP vaccines do and will continue to cause undesirable effects[, including seizures], albeit at reduced frequency and severity compared with [DTwP] vaccines." Id. at 46–47 (quoting Pet'rs' Ex. 138, at 7, ECF No. 97-2).[6] An abstract by Jackson et al. includes similar findings. See id. at 47 n.19 (citing Pet'rs' Ex. 140, 1–2, ECF No. 97-4).[7]

Braun et al. noted that seizures were a known side effect of both the DTwP and DTaP vaccines. See id. at 47 (citing Pet'rs' Ex. 139, at 4, ECF No. 97-3).[8] But of the thirty-four post-DTaP seizures reported in the Vaccine Adverse Event Reporting System that Braun et al. studied, "none of the [study subjects] were reported to have developed a seizure disorder or epilepsy." See id. (quoting Pet'rs' Ex. 139, at 4).

Another study that Petitioners cited—Le Saux et al.—"found a 79% decrease in febrile seizures associated with receipt of [the DTaP] vaccine" compared to the DTwP vaccine. See Pet'rs' Ex. 137, at e348, ECF No. 97-1; Pet'rs' MJAR at 5.[9] But since Le Saux et al. only examined hospitalizations for febrile seizures, the Special Master found that their research did not meaningfully contribute to his analysis because it did not include any long-term follow-up to determine whether any study subjects subsequently developed a seizure disorder. See Dec. at 48 (citing Pet'rs' Ex. 137, at e348).

These studies support the theory that there is an association between the DTaP vaccine and postimmunization seizures, albeit less than was true with the DTwP vaccine. But, as Dr. Raymond observed, they do not provide any support for Petitioners' theory that the vaccine can cause a recipient to develop a seizure disorder, such as Dravet syndrome. See Resp't's Ex. D, at 3, ECF No. 128-1 (report of Dr. Raymond's emphasizing that "none of the[se] studies state that

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[6] Although Petitioners' Exhibit 138, ECF No. 97-2, was filed without bibliographic information, the Special Master determined that the appropriate citation is: Dennis A. Conrad & Hal B. Jenson, Using Acellular Pertussis Vaccines for Childhood Immunization: Potential Benefits Far Outweigh Potential Risk, 105 Postgraduate Med. 165 (1995).

[7] The full citation for Petitioners' Exhibit 140, ECF No. 97-4, is: Lisa Jackson et al., Retrospective Population-Based Assessment of Medically Attended Injection Site Reactions, Seizures, Allergic Responses and Febrile Episodes After Acellular Pertussis Vaccine Combined with Diphtheria and Tetanus Toxoids, 21 Pediatric Infectious Disease J. 781 (2002).

[8] The full citation for Petitioners' Exhibit 139, ECF No. 97-3, is: M. Miles Braun et al., Infant Immunization with Acellular Pertussis Vaccines in the United States: Assessment of the First Two Years' Data from the Vaccine Adverse Event Reporting System (VAERS), 106 Pediatrics e51 (2000).

[9] The full citation for Petitioners' Exhibit 137, ECF No. 97-1, is: Nicole Le Saux et al., Decrease in Hospital Admissions for Febrile Seizures and Reports of Hypotonic-Hyporesponsive Episodes Presenting to Hospital Emergency Departments Since Switching to Acellular Pertussis Vaccine in Canada: A Report from IMPACT, 112 Pediatrics e348 (2003).

epilepsy or an ongoing seizure disorder occurs as an adverse event following immunization with any pertussis containing vaccine"). Rather, the Special Master found, the evidence shows that Dravet syndrome is caused by a defect in the SCN1A gene. Dec. at 74. And in deciding whether Petitioners made a prima facie case under Althen, it is appropriate to consider all evidence, including that of alternative cause. See Sharpe, 964 F.3d at 1082.

The Court concludes, therefore, that the Special Master reasonably found that Petitioners failed to provide a sound and reliable medical or scientific basis to support their theory that the DTaP vaccine can cause recipients to develop seizure disorders, including Dravet syndrome. Accordingly, his finding that Petitioners failed to satisfy Althen prong 1 was neither arbitrary and capricious nor contrary to law.

B. The Special Master's Finding that Petitioners Failed to Supply a Sound and Reliable Medical Theory to Explain How the DTaP Vaccine Could Have Aggravated A.V.'s Seizure Disorder (Loving Prong 4)

In addition to rejecting Petitioners' argument that the DTaP vaccine can cause a recipient to develop a seizure disorder like Dravet syndrome, the Special Master concluded that Petitioners failed to provide a sound and reliable medical theory to explain how the vaccine might aggravate or worsen such a disorder. See Dec. at 49, 52, 74. Therefore, he found, Petitioners failed to satisfy Loving prong 4. Id. at 52.

In so finding, the Special Master credited the opinion of the government's expert, Dr. Raymond, and rejected the opinions of Petitioners' medical experts, Drs. Boles and Kinsbourne. Cf. Dec. at 49, 52 with id. at 74. Drs. Boles and Kinsbourne acknowledged that the mutation in A.V.'s SCN1A gene caused alterations in her neurophysiology that increased her risk of developing Dravet syndrome. See Pet'rs' Ex. 45, at 7; Pet'rs' Ex. 82, at 5; Pet'rs' Ex. 153, at 1, ECF No 121-2. But in their view, exposure to an environmental factor, such as a vaccine or viral infection, is necessary to trigger the disorder's onset. See Pet'rs' Ex. 82, at 7–9, 13; Pet'rs' Ex. 45, at 7–10; Pet'rs' Ex. 46, at 1–2. They also opined that whether—and with what severity—A.V. would develop Dravet syndrome, turned on if—and how early in life—she encountered the environmental factor. See Oral Arg. Tr. at 11, 19–20; Pet'rs' Ex. 45, at 7–9, 12; Pet'rs' Ex. 46, at 1; Pet'rs' Ex. 82, at 4–9, 13; Pet'rs' Ex. 153, at 1–2.

In the views of Drs. Kinsbourne and Boles, research in genetics, animal models, and human studies all demonstrate that the earlier onset of seizures in children with Dravet syndrome results in worsened clinical outcomes. See Pet'rs' Ex. 45, at 13 (Dr. Kinsbourne opining that A.V.'s Dravet syndrome "would have been less severe had the [DTaP] vaccination[] not triggered the onset of her seizure disorder" "at seven months of age"); Pet'rs' Ex. 82, at 13 (Dr. Boles opining that "if [A.V.] had not been vaccinated [with DTaP], . . . her outcome would have been better than it is today").

Also citing animal models as well as studies of children with the SCN1A mutation, Dr. Raymond disagreed with the opinions of Drs. Boles and Kinsbourne that earlier onsets of seizure disorders negatively impact clinical outcomes. See Resp't's Ex. C, at 6, 9, ECF No. 77-1. He emphasized that "while . . . [a] fever may occur in young children following vaccination as an adverse event, . . . [no] studies state that [Dravet syndrome] occurs as an adverse event following immunization with [DTaP]." Resp'ts' Ex. D, at 3. He added further that "an overwhelming body of scientific literature" continues to show that the timing of the first seizure does not "alter[] the

tragic course of this genetic disorder." See Resp'ts' Ex. A, at 6. In Dr. Raymond's view, the variability in outcomes that are experienced by individuals with the mutation of the SCN1A gene can be explained by differences in the nature of the mutations, as opposed to environmental factors. See Resp't's Ex. C, at 9–10, 14.

The Special Master also engaged in a detailed discussion of the medical literature on which the competing experts relied. See Dec. at 53–70. Ultimately, he found Dr. Raymond's views more persuasive than the opinions of Petitioners' medical experts, Drs. Kinsbourne and Boles. See id. at 74. He reasoned that Dr. Raymond "has more experience treating children and their families for genetic-based neurologic problems" and "supported his opinion that a mutation in A.V.'s SCN1A gene '[wa]s the sole cause of her [seizure disorder]'" more persuasively than Petitioners' experts supported their own. Id. at 74 (quoting Resp't's Ex. D, at 3).

In their Motion for Review, Petitioners criticize the Special Master's finding that the studies performed by Brunklaus et al. and McIntosh et al. supported Dr. Raymond's opinion. See Pet'rs' Mot. for Rev. II, at 6–8. The Brunklaus article, Petitioners contend, does not show that the SCN1A mutation was the sole cause of A.V.'s injury because the study was too small. Id. at 6–7. Petitioners further note that the McIntosh article, which found that vaccinations have no long-term impacts on outcomes of Dravet syndrome, has been criticized as invalid by Petitioners' statistical expert, Dr. McNulty. Id. at 7–8.

Of course, these were not the only two studies that the Special Master considered when he addressed whether the DTaP vaccine can aggravate an existing seizure disorder. As he observed, "[m]ultiple groups have explored whether childhood vaccines cause or worsen seizures in children with SCN1A mutations." Dec. at 70. Investigators have used a variety of approaches, and yet they "have not detected any evidence that vaccines alter the child's seizure pattern." Id. Instead, he observed, "the large studies tend to show that the genetic mutation causes the seizures." Id.

As the court of appeals has noted, "[f]inders of fact are entitled—indeed, expected—to make determinations as to the reliability of the evidence presented to them." Moberly, 592 F.3d at 1326. It has explained that:

> Congress assigned to a group of specialists, the Special Masters within the Court of Federal Claims, the unenviable job of sorting through these painful cases and, based upon their accumulated expertise in the field, judging the merits of the individual claims. The statute makes clear that, on review, the Court of Federal Claims is not to second guess the Special Masters['] fact-intensive conclusions; the standard of review is uniquely deferential for what is essentially a judicial process . . . . That level of deference is especially apt in a case in which the medical evidence of causation is in dispute.

Deribeaux v. Sec'y of Health & Hum. Servs., 717 F.3d 1363, 1366–67 (Fed. Cir. 2013) (quoting Hodges, 9 F.3d at 961); see also de Bazan v. Sec'y of Health & Hum. Servs., 539 F.3d 1347, 1354 (Fed. Cir. 2008) (upholding the special master's determination that respondent's expert testimony was more credible and probative than that of the petitioner's expert); Lampe v. Sec'y of Health & Hum. Servs., 219 F.3d 1357, 1361–62 (Fed. Cir. 2000) (upholding the special master's determination that the Secretary's medical expert was more persuasive than the petitioners' medical expert because "[t]hose findings, which are at the core of the special

master's decision in this case, are largely based on his assessments of the credibility of the witnesses and the relative persuasiveness of the competing medical theories of the case. As such, they are virtually unchallengeable on appeal.").

The Special Master here drew upon his expertise in the field, and, giving greater weight to the opinions of Dr. Raymond, found no reliable medical or scientific basis for Petitioners' theory that a DTaP vaccine can aggravate or worsen the condition of an individual with Dravet syndrome. And because Petitioners failed to satisfy both Althen prong 1 and Loving prong 4, the Special Master acted within his discretion when he found that they failed to establish a prima facie case that the DTaP vaccine either caused or aggravated A.V.'s seizure disorder.

C. The Special Master's Finding that Petitioners Failed to Prove a Logical Sequence of Cause and Effect Showing that the DTaP Vaccine Caused or Aggravated A.V.'s Seizure Disorder (Althen Prong 2/Loving Prong 5)

As described above, in addition to supplying a reliable scientific or medical basis for their theory of causation, Petitioners must show under Althen prong 2 and Loving prong 5 that there is a "logical sequence of cause and effect" between receiving the DTaP vaccine and the development or aggravation of Dravet syndrome. Sharpe, 964 F.3d at 1085; see also Capizzano v. Sec'y of Health & Hum. Servs., 440 F.3d 1317, 1324 (Fed. Cir. 2006) (quoting Althen, 418 F.3d at 1278); Pafford v. Sec'y of Health & Hum. Servs., 451 F.3d at 1356 (Fed. Cir. 2006) (stating that "petitioner[s] must show that the vaccine was the 'but for' cause of the harm . . . or in other words, that the vaccine was the 'reason for the injury'"). The sequence of cause and effect must be "'logical' and legally probable, not medically or scientifically certain." Knudsen, 35 F.3d at 548–49.

As noted above, Petitioners' theory is that the DTaP vaccine aggravated A.V.'s Dravet syndrome because it induced the initial febrile seizure, which caused brain injury that triggered or at least accelerated the onset of her seizure disorder. See Pet'rs' Ex. 45, at 7; Pet'rs' Ex. 82, at 5; Pet'rs' Ex. 153, at 1. The Special Master rejected Petitioners' argument that this theory provides a logical sequence of cause and effect between the DTaP vaccine and either the development or aggravation of A.V.'s seizure disorder. See Dec. at 48–49.

The primary flaw in this theory, according to the Special Master, was that there was no evidence that A.V. suffered a brain injury as a result of her initial seizure. Id. at 50. He observed that A.V. was examined by her pediatrician, Dr. Subramanian, and had a consultation with Dr. Ikramuddin, a pediatric neurologist, shortly after her initial seizure. See Dec. at 33–34; see also Pet'rs' Ex. 11, at 28; Pet'rs' Ex. 10, at 65. The Special Master explained that neither of these "treating doctor[s]" "indicated that the vaccination caused any lasting harm to A.V." Dec. at 49 (emphasis added) (citing Oral Arg. Tr. 37:6–38:12; Pet'rs' MJAR at 9; Pet'rs' Reply to Resp't's Resp. to MJAR at 2); see also Pet'rs' Ex. 11, at 28–29; Pet'rs' Ex. 10, at 65. To the contrary, the "immediate effects [of A.V.'s initial febrile seizure] dissipated within a few days," Dec. at 49, and it was not until she developed a fever from a confirmed viral infection nearly three months later that she experienced another seizure, id. at 51 (citing Pet'rs' Ex. 11, at 25).

The Special Master appropriately gave substantial weight to the fact that A.V.'s treating physicians believed that A.V. had not suffered lasting, much less permanent, harm as a result of the vaccine-induced seizure. As the court of appeals has observed, "medical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best

position to determine whether 'a logical sequence of cause and effect show[s] that the vaccination was the reason for the [significant aggravation of the condition at issue].'" Capizzano, 440 F.3d at 1326 (quoting Althen, 418 F.3d at 1280); see also Andreu, 568 F.3d at 1375.

Further, A.V. exhibited no clinical signs of recent seizure activity just hours after her initial seizure. During her brief hospital stay, A.V.'s temperature returned to normal, and her head CT scan, EEG study, and routine blood testing were all unremarkable. See Pet'rs' Ex. 1 pt. 2, at 57, 76, 88; see also Pet'rs' Ex. 3 pt. 2, at 69, 78 (reflecting A.V.'s discharge less than forty-eight hours after arriving at the ED). She also exhibited "no evidence of altered mental status or . . . encephalopathy" shortly after her initial seizure. See Dec. at 50 (quoting Resp't's Ex. C, at 2).

Because A.V. did not show any signs of brain injury after her initial febrile seizure, Dr. Raymond reported that it was his opinion, "to a reasonable degree of medical certainty," that A.V.'s Dravet syndrome "was n[either] caused nor exacerbated by any of the immunizations that she received." See Resp't's Ex. C, at 15. The Special Master credited Dr. Raymond's opinion, because Petitioners did not "counter[] the contention that A.V. returned to her baseline shortly after [her initial febrile seizure]." Dec. at 50. Further, he found that neither Dr. Kinsbourne nor Dr. Boles attempted to reconcile A.V.'s normal EEG and CT scan with their theory that the vaccine-induced initial seizure caused A.V. to suffer brain injury. Id.

Petitioners argue in their Motion for Review that it is of no moment that the EEG study and CT scan showed no evidence that A.V. suffered brain injury after the DTaP vaccine induced her first febrile seizure. See Pet'rs' Mot. for Rev. II at 1, 3–4. They observe that under the diagnostic criteria for Dravet syndrome, EEG studies are initially normal until additional seizures have occurred over several months. See id. They also observe that none of A.V.'s treating physicians or experts "reached the conclusion that the first seizure was not related to her long-term seizure disorder." See id. at 3.

Petitioners' observations miss the mark. Neither the Special Master nor Dr. Raymond denied that the seizure A.V. suffered after she received the DTaP vaccine was "related" to her Dravet syndrome. To the contrary, as Dr. Raymond explained, "[f]ebrile seizures are common as the initial manifestation of Dravet syndrome and may be secondary to any event which raises the child's temperature." Resp't's Ex. D, at 3. He was of the view, however, that the vaccine did not cause A.V.'s Dravet syndrome, and that her rapid return to baseline after the initial seizure showed that the vaccine did not make her seizure disorder worse. See id.

In short, A.V.'s medical records reflect that she rapidly recovered after her initial seizure. They provide no evidence that she suffered brain damage as a result of the initial seizure; indeed they show that she did not. The Special Master's conclusion—that Petitioners did not establish that the DTaP vaccine "was the logical reason for the . . . worsening of A.V.'s seizure disorder"—was not arbitrary and capricious but was instead consistent with A.V.'s medical records and the opinion of the Secretary's expert, Dr. Raymond. See Dec. at 52. Accordingly, the Court has no basis for setting it aside.

CONCLUSION

Based on the foregoing discussion, Petitioners' Corrected Motion for Review, ECF No. 143, is **DENIED**, and the Special Master's decision is **SUSTAINED**. The Clerk is directed to enter judgment accordingly.

IT IS SO ORDERED.

s/ Elaine D. Kaplan
ELAINE D. KAPLAN
Chief Judge